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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:	)	Group Art Unit: 1634
ADAMS *et al.*	)	Examiner: Chakrabarti, A.
Serial No. 09/867,193	)	Confirmation No. 7798
Filed: May 29, 2001	)	Atty. Docket No. GP100-03.CN1
For: DECOY PROBES	)	**VIA FACSIMILE**

SUBMISSION UNDER 37 C.F.R. § 1.114

Box RCE
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This submission is responsive to the Examiner's Final Office Action mailed on June 20, 2002 in the above-captioned application.

Remarks

Claims 1-18 and 34-39 are presently pending in the subject application.

Reconsideration and allowance in view of the following remarks are respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1-16 and 36-39 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Wright *et al.* (*Science* (1997) 276:614-617) in view of Gold *et al.* (U.S. Patent No. 5,811,533). Applicants respectfully traverse this rejection for the reasons that follow.

Applicants submit that the Examiner cannot rely upon Wright in making out a *prima facie* case of obviousness because the objective of Wright was coupled catalysis and amplification. Any modification of the molecule in Wright which would render a terminal 3' OH group unavailable

to accept a nucleoside triphosphate in a polymerization reaction, as presently claimed, would be directly contrary to Wright's stated objective. *See* MPEP § 2143.03 at 2100-126 (8th ed., August 2001) ("To establish *prima facie obviousness* of a claimed invention, all the claim limitations must be taught or considered.") (Emphasis added.) Even so, Applicants submit that the Examiner has failed to identify where it is that Gold teaches modifying a disclosed ligand so that there is no terminal 3' OH group available to accept a nucleoside triphosphate in a polymerization reaction.

In response to this argument, the Examiner has suggested that Table 4 of Gold teaches blocking the 3' OH group to inhibit a polymerase reaction. Applicants have reviewed Table 4 of Gold and the supporting description and have been unable to identify any disclosure which would support the Examiner's interpretation. While SEQ ID Nos. 153 and 154 of Table 4 are shown to include 3' phosphorothioate groups, Applicants note that a phosphorothioate oligonucleotide is one in which a phosphate oxygen atom has been replaced by a sulfur atom. *See* Uhlmann *et al.*, "Antisense Oligonucleotides: A New Therapeutic Principle," *Chemical Reviews*, 90(4):543-584 (1990). (A copy of this reference is included with Applicants' Supplemental Information Disclosure Statement filed therewith.) The 3' OH group is not blocked in a phosphorothioate oligonucleotide. Morever, Gold does not teach that the purpose of this modification is to inhibit a polymerase reaction, as the Examiner contends, (*see* Final Action at page 8, first full paragraph), but rather "to inhibit the activity of exonucleases and endonucleases." *See* Gold at col. 13, lines 4-6.

Additionally, the Examiner's response fails to consider the combination of references which form the basis of this rejection. Instead of identifying any motivation for modifying Wright, which teaches a molecule for use in an amplification reaction, the Examiner's remarks are limited to an incorrect conclusion that Gold teaches blocking a 3' OH group to inhibit a polymerase reaction. And even if Gold did teach blocking a 3' OH group to make it unavailable to accept a nucleoside triphosphate in a polymerization reaction, the Examiner has never identified any motivation for modifying the molecule disclosed by Wright so that it, contrary to its intended purpose, could not

be used to initiate an amplification reaction. *See* MPEP § 2143.01 at 2100-123 (8th ed., August 2001) ("Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art."). Applicants submit that the Examiner's failure to identify and articulate any motivation for combining the cited references to arrive at Applicants' claimed invention indicates that the Examiner has engaged in improper hindsight reasoning. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 17 and 18 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Wright *et al.* (*Science* (1997) 26:614-617) in view of Gold *et al.* (U.S. Patent No. 5,811,533), and further in view of Olson *et al.* (U.S. Patent No. 5,861,273). Applicants respectfully traverse this rejection for the reasons that follow.

Wright and Gold are cited in combination for teaching the decoy probe of claims 1-16 for the reasons set forth in paragraph 4 of the Examiner's Final Action. While conceding that neither Wright nor Gold teaches a nucleotide base recognition sequence region having nucleotide base similarity of at least 75% with at least one of SEQ ID Nos. 1, 2, 3, 4, 5 and 6, the Examiner nevertheless contends that the sequence of SEQ ID NO:3 of the presently claimed invention is identical to the sequence of SEQ ID NO:4 of Olson. Applicants submit that any showing of sequence similarity between the sequences of the claimed invention and Olson would be inadequate to overcome the deficiencies noted above in the Wright and Gold references.

The Examiner's response to this argument is limited to the teachings of Olson alone. Thus, as a first matter, Applicants respectfully submit that the Examiner has failed to heed his own admonishment not to consider the references individually. Second, the Examiner contends that Applicants have argued that the motivation of Olson is different from that of Applicants. A review

of Applicants' previous and current arguments will show that Applicants have never argued the "motivation" of Olson, only that this secondary reference could not be used to overcome the deficiencies noted in the combined teachings of Wright and Gold. Applicants submit that the Examiner has still provided no reasoned explanation indicating how the combined teachings suggest the claimed decoy probes, with all of their limitations. *See* MPEP § 2143.03 at 2100-126 (8th ed., August 2001). Accordingly, withdrawal of this rejection is respectfully requested.

Claims 34 and 35 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Wright *et al.* (*Science* (1997) 26:614-617) in view of Gold *et al.* (U.S. Patent No. 5,811,533), and further in view of Stackebrandt *et al.* (U.S. Patent No. 5,089,386). Applicants respectfully traverse this rejection for the reasons that follow.

Wright and Gold are cited in combination for teaching the decoy probe of claims 1-16 for the reasons set forth in paragraph 4 of the Examiner's Final Action. While acknowledging that Wright in view of Gold do not teach a decoy probe containing a region of self-complementarity, the Examiner contends that Stackebrandt teaches the decoy probe of the claimed invention having a region of self-complementarity. Applicants first submit that the Examiner has failed to establish that Stackebrandt teaches anything but probes which may exhibit a degree of self-complementarity. Contrary to the Examiner's suggestion, Stackebrandt provides no definition of a probe which meets the requirements of the claimed decoy probes. *See* Stackebrandt at col. 2, lines 16-20. Additionally, the Examiner has quoted Stackebrandt out of context. What Stackebrandt actually teaches is that probes to structured regions may themselves have regions of self-complementarity. Therefore, Stackebrandt concludes that it is important to *minimize* such self-complementarity because "self-complementary probes can render themselves inaccessible for hybridization to their target sequences." *See* Stackebrandt at col. 6, lines 32-51. Thus, Stackebrandt, if anything, provides a teaching away from probes having regions of self-complementarity. *See* § 2141.02 at 2100-120 (8th

ed., August 2001) ("A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.") (Emphasis added.)

Responding to this argument, the Examiner submits that Applicants have argued that "at no place in the referred [to] text of Stackebrandt is [*sic,* are] probes [disclosed] which may exhibit self-complementarity." *See* Final Action at page 8, lines 13-15. This is flatly wrong. What Applicants have instead argued is that probes targeting structured regions of a targeted nucleic acid may have regions of self-complementarity, and that such probes are generally to be avoided because they may hybridize to themselves rather than to the targeted nucleic acid. Based on this teaching away from the use of self-complementary detection probes for targeting structured nucleic acids, the Examiner has failed to establish what *motivation* there would have been for including a region of self-complementarity in the claimed decoy probes, with all of their limitations.

Additionally, the Examiner has never established what the *motivation* would have been for including a region of self-complementarity in the promoter sequence-containing molecules of Wright, the primary reference relied upon by the Examiner in making out this rejection. *See* MPEP § 2143.01 at 2100-123 (8th ed., August 2001). Accordingly, Applicants submit that Stackebrandt adds nothing to the teachings of Wright and Gold and, in fact, specifically teaches away from designing probes to include regions of self-complementarity. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

Applicants submit that the subject application is in condition for allowance and Notice to that effect is respectfully requested.

Please charge any fees due in connection with this Submission to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

SUBMISSION

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Certificate of Transmission

I hereby certify that this correspondence (and any referred to as attached) is being sent by facsimile to 703-872-9307 on the date indicated below to Box RCE, Assistant Commissioner for Patents, Washington, D.C. 20231.

Respectfully Submitted,

Date: June 25, 2002 By: _____

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